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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, L.L.P.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
STOCKTON, LAURA LYNNE	
ART UNIT	**PAPER NUMBER**
1626	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/585,635	QUATTROPANI ET AL.	
	Examiner	Art Unit	
	LAURA L. STOCKTON	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-6, 8-11, 13-15 and 17-27* is/are pending in the application.

4a) Of the above claim(s) *18-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-6,8-11,13-15,17,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/13/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 2-6, 8-11, 13-15 and 17-27 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-17 and 26 – drawn to products of formula (I) wherein **X** is S) in the reply filed on July 15, 2009 was acknowledged in a previous Office Action. The requirement was deemed proper and therefore made FINAL in a previous Office Action.

Subject matter not embraced by elected Group I and Claims 18-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the

restriction (election) requirement in the reply filed on July 15, 2009.

Information Disclosure Statement

The Examiner has considered the Information Disclosure Statement filed on January 13, 2011. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

The rejections and objections made in the previous Office Action that do not appear below have been overcome by Applicant's amendments to the claims. Therefore, arguments pertaining to these rejections and objections will not be addressed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 9 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 lacks antecedent basis from currently amended claim 2 since the R^6 variable in currently amended claim 2 does not represent C_1-C_6 alkyl. See claim 11 for same.

Claim 9 lacks antecedent basis from currently amended claim 2 since the R^6 variable in currently amended claim 2 does not represent phenyl.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2-5, 8, 11, 13, 14, 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by:

a) Inaba et al. {JP 2002/53566 A} - Compounds 154 and 155 (reproduced below) on page 31 of 84 of the previously supplied English translation of JP 2002/53566;

b) Chemical Abstracts Registry Number 472981-38-7 {indexed in the Registry file on STN CAS ONLINE November 11, 2002};

d) Chemical Abstracts Registry Number 472981-35-4 {indexed in the Registry file on STN CAS ONLINE November 11, 2002};

i) Chemical Abstracts Registry Number 472979-27-4 {indexed in the Registry file on STN CAS ONLINE November 11, 2002;

n) Chemical Abstracts Registry Number 368859-44-3 {indexed in the Registry file on STN CAS ONLINE November 12, 2001;

o) Chemical Abstracts Registry Number 368857-86-7 {indexed in the Registry file on STN CAS ONLINE November 12, 2001;

q) Chemical Abstracts Registry Number 368857-82-3 {indexed in the Registry file on STN CAS ONLINE November 12, 2001]; or

s) Suciu et al. {CA 75:35865, 1971} - see the compound of CA Registry No. 32519-86-1.

Each of the above cited prior art disclose at least one compound which is embraced by the instant claimed invention. Note on page 18, lines 18-25, of the instant specification, it states that the compounds of Formula (I) embrace pharmaceutical acceptable salts of compounds of Formula (I). Therefore, each of the above cited prior art anticipates the instant claimed invention.

Response to Arguments

Applicant's arguments filed January 13, 2011 have been fully considered but they are not persuasive. In regard to the rejection of the claims over compounds 154 and 155 in Inaba et al. (page 31 of the English translation), Applicant argues that the instant R^6 variable definition does not embrace a cycloalkyl-carbonyl- and that a C_1-C_6alkyl-C_{3-8}cycloalkyl substituted by oxy is not within the substituents listed in the claims.

Applicant's arguments have been considered but have not been found persuasive. As stated in the previous Office Action, Compounds 154 and 155 (reproduced below)

154	 C15H18N4O2S2
155	 C16H20N4O2S2

are embraced by the instant currently amended claims when R^1 is $-NR^5R^6$; R^5 is hydrogen; R^6 is C_1-C_6 alkyl C_3-C_8 cycloalkyl; R^2 is H; R^3 is C_1-C_6 alkyl; R^4 is C_1-C_6 alkyl; and X is S. Note that on page 16, lines 20-28, of the instant specification (reproduced below),

"Substituted or unsubstituted": Unless otherwise constrained by the definition of the individual substituent, the above set out groups, like "alkenyl", "alkynyl", "aryl", "heteroaryl", "cycloalkyl", "heterocycloalkyl" etc. groups can optionally be substituted with from 1 to 5 substituents selected from the group consisting of "C_1-C_6-alkyl", "C_2-C_8-alkenyl", "C_2-C_8-alkynyl", "cycloalkyl", "heterocycloalkyl", "C_1-C_6-alkyl aryl", "C_1-C_6-alkyl heteroaryl", "C_1-C_6-alkyl cycloalkyl", "C_1-C_6-alkyl heterocycloalkyl", "amino", "ammonium", "acyl", "acyloxy", "acylamino", "aminocarbonyl", "alkoxycarbonyl", "ureido", "aryl", "carbamate", "heteroaryl", "sulfinyl", "sulfonyl", "alkoxy", "sulfanyl", "halogen", "carboxy", trihalomethyl, cyano, hydroxy, mercapto, nitro, and the like.

the substituent groups embrace unsubstituted or substituted unless otherwise constrained. The list of possible substituents substituted on groups such as "alkyl" is open-ended since the paragraph ends with "and the like". Further, claims are not limited to the disclosure of the specification. Claims are given their broadest interpretation and therefore, any substituent can be attached to groups such as "alkyl" because such specific substitution limitations are not found in the claims. So, the instant R^6 variable position of Compounds 154 and 155 is a cycloalkyl-carbonyl wherein the instant C_1-C_6 alkyl C_3-C_8 cycloalkyl substituent, defined by R^6, is a substituted alkyl

(i.e., an alkyl substituted with an oxo). Therefore, Inaba et al. anticipate the instant currently amended claimed invention.

Applicant argues that the instant R^6 variable definition has been amended and therefore, previously cited prior art references (b)-(r) do not anticipate the instant claims. In response, Applicant only amended one independent claim, that being instant claim 2. However, instant claim 27 is also an independent claim which was previously rejected under 35 USC 102(b). The above cited prior art references (b), (d), (i), etc. still anticipate species found in independent previously presented claim 27. See, for example, the tenth species listed on page 22 in claim 27; the twelfth species listed on page 22 in claim 27; etc. For all the reasons given above, the rejection is deemed proper and therefore, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-6, 8-11, 13-15, 17, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inaba et al. {JP 2002/53566 A}, Wu et al. {WO 2006/050351 A2} and Takaya et al. {U.S. Patent 4,649,146}, each taken alone. An English translation was provided of the JP document with a previous Office Action and will be referred to hereinafter.

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicant claims thiazole compounds. **Inaba et al.** (see entire document; particularly page ii of 48 thru page 16 of 48, page 25 of 48 thru page 26 of 48; and especially Compounds 154 and 155 on page 31 of 84), **Wu**

et al. (see entire document; particularly pages 4, 5, 7 and 10-12, and Formula Ic on page 5; and especially Compound Number 2 in Table 1 on page 18) and **Takaya et al.** (see entire document; particularly column 1; formula [Ik] at the top of column 5, lines 1-5; column 11, lines 28-33; column 12, lines 41-45; and especially Examples 85 and 87 in column 46 and Example 123 in column 55) each teach thiazole compounds that are either structurally the same as (see above 102 rejection) or structurally similar to the instant claimed compounds.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between some of the thiazole compounds of the prior art and the compounds instantly claimed is that the instant claimed thiazole compounds are generically described in the prior art.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

The indiscriminate selection of "some" among "many" is *prima facie* obvious, *In re Lemin*, 141 USPQ 814 (C.C.P.A. 1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., protein kinase Cγ inhibitors).

One skilled in the art would thus be motivated to prepare products embraced by the prior art to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be useful as, for example, a pain killer. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

At the very least, such renders at bar obvious as regards these structured compounds and, as regards homologous, isomeric, or other "similar" compounds encompassed in the claims, such are obvious, under 35

U.S.C. § 103 over said reference compounds. In order to establish patentability, there must at least be a comparative showing establishing distinguishing characteristics allegedly showing that claimed compounds are unobvious.

Response to Arguments

Applicant's arguments filed January 13, 2011 have been fully considered but they are not persuasive. Applicant argues that: (1) there is no evidence that one of ordinary skill would have selected the prior art compound as the lead compound; (2) one of ordinary skill must have reason to attempt to make the claimed compound by modifying the lead compound; and (3) there must be a reasonable expectation of success in making the claimed compound.

All of Applicant’s arguments have been considered but have not been found persuasive. As stated in the previous Office Action, the factual inquiries set forth

in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Each of the factual set forth in *Graham* v. *John Deere Co.* have been addressed in the above 35 USC 103 rejection.

Applicant argues that there is no evidence that one of ordinary skill would have selected the prior art compound as the lead compound and that one of ordinary

skill must have reason to attempt to make the claimed compound by modifying the lead compound. In response, the Examiner's position is consistent with the later decision, *Aventis Pharma Deutschland GmbH v. Lupin Ltd.* 84 USPQ2d 1197 (Fed. Cir. 2007), especially the following passage at page 1204: "In the chemical arts, we have long held that "structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions, creates a *prima facie* case of obviousness." *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, No. 06-1329, slip op. at 9 (Fed. Cir. June 28, 2007) (quoting *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990) (en banc)); *see also In re Papesch*, 315 F.2d 381, 137 USPQ 43 (C.C.P.A. 1963). The "reason or motivation" need not be an explicit teaching that the claimed compound will have a particular utility; it is sufficient to show that the claimed and prior art

compounds possess a "sufficiently close relationship … to create an expectation," in light of the totality of the prior art, that the new compound will have "similar properties" to the old. *Dillon*, 919 F.2d at 692; *see also In re Wilder*, 563 F.2d 457, 460 (C.C.P.A. 1977) ("[O]ne who claims a compound, per se, which is structurally similar to a prior art compound must rebut the presumed expectation that the structurally similar compounds have similar properties."). Once such a *prima facie* case is established, it falls to the applicant or patentee to rebut it, for example with a showing that the claimed compound has unexpected properties. *Dillon*, 919 F.2d at 692.".

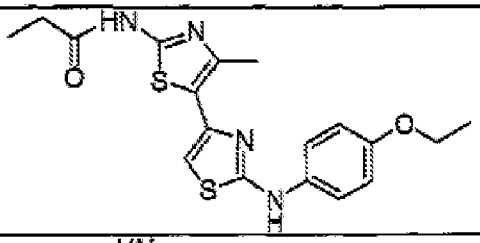
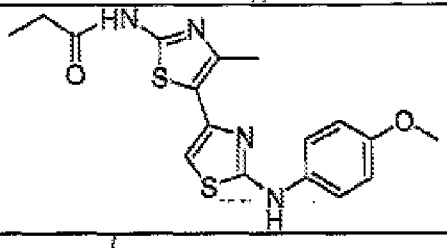
Applicant argues the need for a prior art compound to be characterized as a "lead compound" before any modification to such compound(s) can be made to show obviousness and further seems to assume that the term "lead compound" has been defined by the Court in the same way as a researcher in the pharmaceutical field

might view the term- i.e. as a compound having undergone preclinical and/or clinical trials or being the most active for a given activity. But this term, as evident by the Court in *Eisai Co. Ltd. v. Dr. Reddy's Laboratories Ltd.* 87 USPQ2d 1452 (Fed. Cir. 2008), includes any compound that an examiner or court would use as the basis for a structural obviousness argument. Note the reference to "a **known** compound (i.e., a lead compound)" (bold emphasis added) on page 1455, first full paragraph is not as confining as Applicant's interpretation. Thus, in the Examiner's opinion, there remains no legal basis that a prior art compound selected to show obviousness based on close structural similarity and/or an equivalency teaching must be particularly singled out for its activity. The fact that it is taught to possess activity is sufficient and where there is no extrinsic evidence to doubt its activity, should not be disqualified where the compound has been otherwise shown to be an obvious variant of

Applicant's invention.

The examiner has expressed in the rejection that the sole feature that is different between the instant claimed compounds and some of the compounds of the prior art is that the instant claimed compounds are generically claimed in the prior art. See, for instance, Compound Number 2 in Wu et al. on page 18 (reproduced below)

Table 1

Compound Number	Structure	Physical Data ^{1}H NMR 400 MHz (DMSO-d_6) and/or MS (m/z)
1		(MH^+) 389.1104
2		(MH^+) 375.0947

where the only difference between Compound Number 2 in Wu et al. and the compounds claimed in instant

independent claim 2 is the *para* attachment to the phenyl ring of the methoxy group {i.e., **4**-methoxy} in Compound Number 2 versus a *meta* attachment to the phenyl ring of the methoxy group {i.e., **3**-methoxy} as instantly claimed (see definition of the instant R^6 variable in instant claim 2 and the definitions of the R_3 and n variables in Wu et al. on page 4). Thus, unlike in *Takeda v. Alphapharm*, 492 F.3d 1350, 1361-1362 (Fed. Cir. 2007), only 1 difference exists between prior art and instant compound, which will also lead to active compounds. In *Takeda*, previously cited, the prior art compound relied on by the Examiner in that case was documented in more than one reference and by expert witnesses as having serious side-effects that would be deleterious for its intended purpose. There is no such evidence herein. It is further noted that the Court in *Takeda* relied on the unexpectedly superior properties of appealed compound over compound b. Thus, given the totality of the facts in *Takeda*, the decision

rendered was based on "reasonable expectation" of success in performing the intended use, which in that case led to the disqualification of the prior art compound. Applicant is reminded that the rejection made herein is not solely based on an alleged structural similarity but also the motivation to modify based on the equivalency teachings which include choices needed to arrive at Applicant's claimed compounds. Therefore, Applicant's argument is not persuasive.

Applicant argues that there must be a reasonable expectation of success in making the claimed compound. In response, the evidence for a reasonable expectation of success in making the claimed compound is supplied by the cited prior art references. MPEP 2143.02 states the following:

2143.02 [R-6] Reasonable Expectation of Success Is Required

>A rationale to support a conclusion that a claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ____, ____, 82 USPQ2d 1385, 1395 (2007); *Sakraida v. AG Pro, Inc.*, 425 U.S. 273, 282, 189 USPQ 449, 453 (1976); *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 62-63, 163 USPQ 673, 675 (1969); *Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp.*, 340 U.S. 147, 152, 87 USPQ 303, 306 (1950).

I. < OBVIOUSNESS REQUIRES ONLY A REASONABLE EXPECTATION OF SUCCESS

The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) (Claims directed to a method of treating depression with amitriptyline (or nontoxic salts thereof) were rejected as *prima facie* obvious over prior art disclosures that amitriptyline is a compound known to possess psychotropic properties and that imipramine is a structurally similar psychotropic compound known to possess antidepressive properties, in view of prior art suggesting the aforementioned compounds would be expected to have similar activity because the structural difference between the compounds involves a known bioisosteric replacement and because a research paper comparing the pharmacological properties of these two compounds suggested clinical testing of amitriptyline as an antidepressant. The court sustained the rejection, finding that the teachings of the prior art provide a sufficient basis for a reasonable expectation of success.); *Ex parte Blanc*, 13 USPQ2d 1383 (Bd. Pat. App. & Inter. 1989) (Claims were directed to a process of sterilizing a polyolefinic

Therefore, the burden is shifted to Applicant and Applicant must present persuasive factual evidentiary showing that there was no reasonable expectation of success and that a difference in structure would lead to a different activity. For all the reasons stated above, the rejection is maintained.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains subject matter not embraced by elected Group I {i.e., **X** is O} and claims 18-25 drawn to inventions nonelected with traverse in the reply filed on July 15, 2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:00 am to 2:30 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

/Laura L. Stockton/
Laura L. Stockton, Ph.D.
Primary Examiner, Art Unit 1626
Work Group 1620
Technology Center 1600

March 24, 2011